What is claimed is:

1. An LHRH antagonist, comprising a peptide having a sidechain modified by a dipolar moiety forming a modified peptide, such that the modified peptide has LHRH antagonist activity.

2. The LHRH antagonist of claim 1, wherein the dipolar moiety is selected from the group consisting of ylids, tertiary amine oxides, nitrile oxides, pyridine-N-oxides, and pyridinium zwitterions.

3. The LHRH antagonist of claim 1, wherein the dipolar moiety is an ylid.

4. The LHRH antagonist of claim 1, wherein the dipolar moiety is a pyridine-N-oxide.

5. The LHRH antagonist of claim 1, wherein the dipolar moiety is a pyridinium zwitterion.

6. The LHRH antagonist of claim 1, wherein the peptide comprises about 8 to about 12 residues.

7. The LHRH antagonist of claim 1, wherein the peptide comprises 10 residues.

8. The LHRH antagonist of claim 1, wherein the dipolar moiety modifies residue 6.

9. The LHRH antagonist of claim 1, wherein the LHRH antagonist is a peptide mimetic.

10. A peptide comprising a structure:

A-B-C-D-E-F-G-H-I-J (SEQ ID NO: 1)

wherein

A is pyro-Glu, Ac-D-Nal , Ac-D-Qal, Ac-Sar, or Ac-D-Pal

B is His or 4-Cl-D-Phe

C is Trp, D-Pal, D-Nal, ~~L-Nal-D-Pal(N-O)~~ L-Nal, D-Pal(N-O), or D-Trp

D is Ser

E is N-Me-Ala, Tyr, N-Me-Tyr, Ser, Lys(iPr), 4-Cl-Phe, His, Asn, Met, Ala, Arg or Ile;

F is

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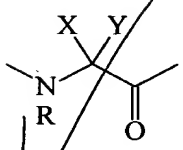


wherein

R and X are, independently, H or alkyl; and

Y comprises a dipolar moiety;

G is Leu or Trp;

H is Lys(iPr), Gln, Met, or Arg

I is Pro; and

J is Gly-NH_2 or D-Ala-NH_2;

or a pharmaceutically acceptable salt thereof.

11. The peptide of claim 10, wherein Y is selected from the group consisting of ylids, tertiary amine oxides, nitrile oxides, pyridine-N-oxides, and pyridinium zwitterions.

12. The peptide of claim 10, wherein Y is an ylid.

13. The peptide of claim 10, wherein Y is a pyridine-N-oxide.

14. The peptide of claim 10, wherein the dipolar moiety is a pyridinium zwitterion.

15. A peptide comprising a structure:
Ac-D-Nal-4-Cl-Phe-D-Pal-Ser-Tyr-D-Pal(N-O)-Leu-Lys(iPr)-Pro-D-Ala-NH_2.

16. A peptide comprising a structure
Ac-D-Nal-4-Cl-D-Phe-D-Pal-Ser-Tyr-D-Pal(CH_2COO^-)-Leu-Lys(iPr)-Pro-D-Ala-NH_2;
or a pharmaceutically acceptable salt thereof.

17. An LHRH antagonist, comprising a peptide having a sidechain modified by a cationic moiety selected from the group consisting of cationic pyridinium moieties and sulfonium moieties, with the proviso that the cationic moiety is not N-methyl pyridinium, forming a modified peptide, such that the modified peptide has LHRH antagonist activity.

18. The LHRH antagonist of claim 17, wherein the cationic moiety is a cationic pyridinium moiety.

19. The LHRH antagonist of claim 17, wherein the cationic moiety is a sulfonium moiety.

20. The LHRH antagonist of claim 17, wherein the peptide comprises about 8 to about 12 residues.

21. The LHRH antagonist of claim 17, wherein the peptide comprises 10 residues.

22. The LHRH antagonist of claim 17, wherein the cationic moiety modifies at least one of residue 6 and residue 8.

23. The LHRH antagonist of claim 17, wherein the LHRH antagonist is a peptide mimetic.

24. A peptide comprising a structure:

A-B-C-D-E-F-G-H-I-J (SEQ ID NO:3)

wherein

A is pyro-Glu, Ac-D-Nal , Ac-D-Qal, Ac-Sar, or Ac-D-Pal

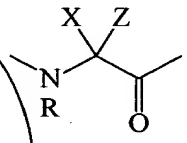
B is His or 4-Cl-D-Phe

C is Trp, D-Pal, D-Nal, L-Nal, D-Pa|(N-O), ~~L-Nal-D-Pal(N-O)~~, or D-Trp

D is Ser

E is N-Me-Ala, Tyr, N-Me-Tyr, Ser, Lys(iPr), 4-Cl-Phe, His, Asn, Met, Ala, Arg or Ile;

F is D-Arg, D-Lys(iPr), D-Pal(iPr), D-Cit or Q, wherein Q has a structure



wherein

R and X are, independently, H or alkyl; and

Z comprises a cationic moiety selected from the group consisting of cationic pyridinium moieties and sulfonium moieties, with the proviso that the cationic moiety is not N-methyl pyridinium;

G is Leu or Trp;

H is Lys(iPr), Gln, Met, Arg or Q;

I is Pro; and

J is Gly-NH_2 or D-Ala-NH_2;

with the proviso that at least one of F and H is Q;

or a pharmaceutically acceptable salt thereof.

25. The peptide of claim 24, wherein F is Q and Z is a cationic pyridinium moiety.

26. The peptide of claim 25, wherein Z is an N-benzyl pyridinium moiety.

27. A peptide comprising a structure
Ac-Sar-4-Cl-D-Phe-D-Nal-Ser-Tyr-D-Pal(Bzl)-Leu-Lys(iPr)-Pro-D-Ala-NH_2;
or a pharmaceutically acceptable salt thereof.

28. The peptide of claim 24, wherein F is Q and Z is a sulfonium moiety.

29. A peptide comprising a structure:
Ac-D-Nal-4-Cl-D-Phe-D-Trp-Ser-Tyr-D-Met(S^+Me)-Leu-Arg-Pro-D-Ala-NH_2;
or a pharmaceutically acceptable salt thereof.

30. The peptide of claim 24, wherein H is Q and Z is a sulfonium moiety.

31. A peptide comprising a structure:
Ac-D-Nal-4-Cl-D-Phe-D-Pal-Ser-Tyr-D-Arg-Leu-Met(S^+Me)-Pro-D-Ala-NH_2;
or a pharmaceutically acceptable salt thereof.

32. An LHRH antagonist, comprising a peptide having a sidechain modified by a receptor-modifying moiety forming a modified peptide, such that the modified peptide has LHRH antagonist activity.

33. The LHRH antagonist of ~~claim~~ 32, wherein the receptor-modifying moiety is selected from the group consisting of ylids, sulfonium moieties, α-halocarbonyls, sulfates, sulfonates alkyl halides, and benzyl halides.

34. The LHRH antagonist of claim 32, wherein the peptide comprises about 8 to 12 residues.

35. The LHRH antagonist of claim 32, wherein the peptide comprises 10 residues.

36. The LHRH antagonist of claim 32, wherein the receptor-modifying moiety modifies residue 6.

37. The LHRH antagonist of claim 32, wherein the LHRH antagonist is a peptide mimetic.

38. A peptide comprising a structure:
A-B-C-D-E-F-G-H-I-J_A (SEQ ID NO: 4)

wherein

A is p-Glu, Ac-D-Nal , Ac-D-Qal, Ac-Sar, or Ac-D-Pal

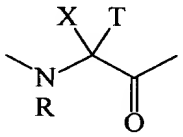
B is His or 4-Cl-D-Phe

C is Trp, D-Pal, D-Nal, L-Nal-D-Pal(N-O), or D-Trp

D is Ser

E is N-Me-Ala, Tyr, N-Me-Tyr, Ser, Lys(iPr), 4-Cl-Phe, His, Asn, Met, Ala, Arg or Ile;

F is



wherein

R and X are, independently, H or alkyl; and

T comprises a receptor-modifying moiety;

G is Leu or Trp;

H is Lys(iPr), Gln, Met, or Arg

I is Pro; and

J is Gly-NH_2 or D-Ala-NH_2;

or a pharmaceutically acceptable salt thereof.

39. The peptide of claim 38, wherein T is selected from the group consisting of ylids, sulfonium moieties, α-halocarbonyls, sulfates, sulfonates, alkyl halides and benzyl halides.

40. The peptide of claim 39, wherein T is an α-halocarbonyl.

41. An LHRH antagonist, comprising a peptide having a sidechain modified by a hydrophilic N-acyl moiety forming a modified peptide, such that the modified peptide has LHRH antagonist activity.

42. The LHRH antagonist of claim 41, wherein the hydrophilic N-acyl moiety modifies position 6.

43. The LHRH antagonist of claim 41, wherein a residue comprises a hydrophilic acyl moiety selected from the group consisting of D-Lys(Imdac), D-Lys(Ppic) and D-Lys(Dodac).

44. The LHRH antagonist of claim 41, wherein the hydrophilic N-acyl moiety has a log P between -1 and +2.

45. A peptide comprising a structure:

A-B-C-D-E-F-G-H-I-J (SEQ ID NO:5)

wherein

A is pyro-Glu, Ac-D-Nal , Ac-D-Qal, Ac-Sar, or Ac-D-Pal

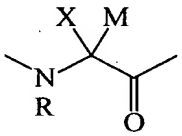
B is His or 4-Cl-D-Phe

C is Trp, D-Pal, D-Nal, L-Nal, D-Pal(N-O), or D-Trp

D is Ser

E is N-Me-Ala, Tyr, N-Me-Tyr, Ser, Lys(iPr), 4-Cl-Phe, His, Asn, Met, Ala, Arg or Ile;

F is



wherein

R and X are, independently, H or alkyl; and

M comprises an N-acyl hydrophilic moiety;

G is Leu or Trp;

H is Lys(iPr), Gln, Met, or Arg

I is Pro; and

J is Gly-NH_2 or D-Ala-NH_2;

or a pharmaceutically acceptable salt thereof.

46. The peptide of claim 44, wherein F is selected from the group consisting of D-Lys(Imdac), D-Lys(Ppic) and D-Lys(Dodac).

47. A peptide comprising a structure:

Ac-D-Nal-4-Cl-D-Phe-D-Pal-Ser-Tyr-D-Lys(Imdac)-Leu-Lys(iPr)-Pro-D-Ala-NH_2;

or a pharmaceutically acceptable salt thereof.

48. An LHRH antagonist, comprising a peptide having a small polar moiety in position 6, such that the peptide has LHRH antagonist activity.

49. The LHRH antagonist of claim 48, wherein the antagonist has an AOA less than about 1 μg.

50. The LHRH antagonist of claim 48, wherein the antagonist has a histamine-releasing activity of at least about 5 μg.

51. A peptide comprising a structure:

A-B-C-D-E-F-G-H-I-J

wherein

A is pyro-Glu, Ac-D-Nal , Ac-D-Qal, Ac-Sar, or Ac-D-Pal

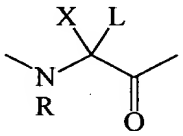
B is His or 4-Cl-D-Phe

C is Trp, D-Pal, D-Nal, L-Nal-D-Pal(N-O), or D-Trp

D is Ser

E is N-Me-Ala, Tyr, N-Me-Tyr, Ser, Lys(iPr), 4-Cl-Phe, His, Asn, Met, Ala, Arg or Ile;

F is



wherein

R and X are, independently, H or alkyl; and

L comprises a small polar moiety;

G is Leu or Trp;

H is Lys(iPr), Gln, Met, or Arg

I is Pro; and

J is Gly-NH_2 or D-Ala-NH_2;

or a pharmaceutically acceptable salt thereof.

52. The peptide of claim 51, wherein L is selected from the group consisting of D-Cit, D-Asn, D-Gln, and D-Thr.

53. A peptide comprising a structure:

Ac-D-Nal-4-Cl-D-Phe-D-Pal-Ser-N-Me-Tyr-D-Asn-Leu-Lys(iPr)-Pro-Ala-NH_2;

or a pharmaceutically acceptable salt thereof.

54. A peptide comprising a structure:

Ac-D-Nal-4-Cl-D-Phe-D-Pal-Ser-Tyr-D-Asn-Leu-Lys(iPr)-Pro-Ala-NH_2;

or a pharmaceutically acceptable salt thereof.

55. A pharmaceutical composition comprising a peptide having a sidechain modified by a dipolar moiety forming a modified peptide, such that the modified peptide has LHRH antagonist activity, and a pharmaceutically acceptable carrier.

56. A method of inhibiting LHRH activity in a subject, comprising administering to a subject an effective amount of the LHRH antagonist of claim 1, such that LHRH activity is inhibited.

57. A method of inhibiting LHRH activity in a cell, comprising contacting a cell with the LHRH antagonist of claim 1, such that LHRH activity is inhibited.

58. A method of inhibiting growth of a hormone-dependent tumor in a subject, comprising administering to a subject an effective amount of the LHRH antagonist of claim 1, such that tumor growth is inhibited.

59. A method of inhibiting ovulation in a subject, comprising administering to a subject an effective amount of the LHRH antagonist of claim 1, such that ovulation is inhibited.

60. A packaged formulation for treating a subject for a disorder associated with LHRH activity, comprising an LHRH antagonist of claim 1 packaged with instructions for using the LHRH antagonist for treating a subject having a disorder associated with LHRH activity.

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